Unclassified
(Security Classification)

Contractor: Army Chemical Center

Contract No: DA 18-108-405-CML-754

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(Indicated type report, i.e.
First Monthly Progress Report,
Second Bimonthly Progress Report,
Final Report, etc.) Semi-Annual REPORT

Covering the Period

1 October 1960 through 31 March 1961

Title: Research on Neuropathological Effects of Military Chemicals

Prepared By

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Enclosure 1

SEMI-ANNUAL PROGRESS REPORT

1 October 1960 through 31 March 1961

Contract #DA 18-108-405-CML-754

PERSONNEL:

The following persons worked under the contract:
Dr. Richard Lindenberg - Principal Investigator, Dr. Angel Pentschev - Senior Investigator, Dr. Thomas Preziosi - Research Associate, Dr. Donald Levy - Research Associate, and Mrs. Leontina Fay - Laboratory Technician I, who started work in November 1960, replacing Mr. Paul Rosdon.

RESEARCH:

The main purpose of the work done under this contract is to re-examine which concentration of CO in the air can be tolerated by healthy individuals for a prolonged period of time without producing permanent organic damage. The various patterns of such damage are known. However, more information is wanted in regard to the factors responsible for the development of lesions and in regard to any causal interrelationship among the lesions themselves. It was, therefore, decided to perform the experimental work in two steps. The first step consisted of single exposures of various length to different concentrations of CO under the best possible control of physiological reactions in order to gain a better insight into the mechanism of the lesions. The second step is planned to consist of long term exposures of groups of animals to CO concentrations critical for the occurrence of permanent damage and below such level. The exposures are planned to be of continuous as well as interrupted type. In pursuing this plan, it is believed that groundwork would be laid also for future studies concerning preventive and therapeutic measures.

The work during the last half year was devoted to single exposures to CO of various concentrations and of various durations. For the matter of comparison,

some animals were exposed to oxygen deficiency equivalent to certain levels of CO hypoxia. During the six month period ending 31 March 1961, 23 dogs were used and the total of experiments since the beginning of the contract amount to the total of 27 dogs.

The attached table gives information for each experiment as to the concentration of CO or O_2, the duration of exposure, the maximum CO saturation in the blood during the experiment, the survival time and the absence or presence of pathologic tissue alterations.

In all experiments the rate of respiration and of pulse were continuously measured. Electrocardiograms were taken. In 15 experiments, the arterial and venous blood pressures were registered and in 19 experiments electroencephalograms were taken. In 12 experiments, the cerebral spinal fluid pressure was recorded and in 10 cases the pressure of the brain against the skull. In every case, blood samples were taken before and during exposure for determinations of hemoglobin, hematocrit, cell count and differential, glucose, sodium and potassium and CO saturation. In most cases, samples were also taken shortly after the exposure for the same type of analysis.

A few interesting and perhaps significant physiological observations may be mentioned. In all cases of CO poisoning, the electrocardiogram soon showed alterations ranging from moderate to very severe, which in case of longer survival, often persisted for several days. As a rule, the electroencephalogram showed pathologic tracings only after the electrocardiogram displayed abnormal features. Furthermore, the pressure of the cerebral spinal fluid or of the brain against the skull started to rise first and this was followed after an interval of a few minutes by a rise in venous pressure. In those cases in which the electroencephalogram showed absence of electrical potentials for more than 5 minutes, the brain revealed pathology except, of course, in those cases which died at the end of the experiment because of respiratory failure.

The pathological examination concerned central nervous system as well as internal organs. As regards the brain, the most severe pathologic finding was a complete necrosis of the entire white matter of the cerebrum as occasionally observed in human beings. In this experiment, the electroencephalogram showed no potentials for about 55 minutes (Exper. No. 15). In addition to the brain, the heart showed diffuse fatty degeneration of muscle fibers, predominantly in the wall of the right ventricle facing the ventricular cavity and in the interventricular septum. The next case in severity with identical distribution of lesions was Exper. No. 18. In all the other cases showing pathology, the lesions were also in the white matter, and there was no case in which nerve cells underwent necrosis. As of now, the evaluation of clinical and pathologic data leads to the conclusion that the heart suffers first, functionally and occasionally also organically, and that this dysfunction of the systemic circulation constitutes an essential factor in the production of lesions in the brain. If further individual exposures corroborate this impression, it indicates that in chronic exposures attention must be given especially to the heart. It also would open up the possibility of preventive and therapeutic treatment with drugs supporting and activating the systemic circulation.

TABLE I

No. Of Experiment	CO% In Air O_2% In Air	Duration Of Exposure	Max. CO Blood Level During Exposure	Survival Time	Pathology
1	1%	11 min.	30%	None	No pathology.
2	1%	10½ min.	37.2%	6 days	Minor pathology in brain.
3	1%	13½ min.	51.6%	6 days	No pathology.
4	1%	8 min. 39 sec.	57.4%	None	No pathology.
5	1%	4 min.	36.9%	95 min.	Venous congestion in all organs.
6	0.5%	19 min. 56 sec.	53%	3 days	No pathology.
7	0.56%	5 min. 25 sec.	47%	None	No pathology.
8	0.43%	18 min. 40 sec.	58.3%	1 min. - 26 sec.	Venous congestion in all organs.
9	0.43%	13 min. 45 sec.	55.8%	3 days	Marked pathology in brain.
10	0.43%	19 min. 23 sec.	56.1%	3 days	Pathology similar to 9.
11	0.43%	11 min. 55 sec.	not determined	3 days	Pathology similar to 9.
12	0.24%	17 min.	61.6%	7 sec.	Organs not studied.
13	0.24%	53 min. 52 sec.	39.5%	7 days	Severe pathology in brain.
14	.248%	88 min. 24 sec.	38.7%	7 days	Pathology similar to 13.
15	0.16%	ca. 290 min.	36.9%	3 days	Most severe pathology in brain and heart.
16	0.16%	112 min.	38.4%	132 min. - 23 sec.	No pathology.
17	0.128%	91 min. 58 sec.	71.2%	None	Venous congestion in all organs.
18	0.128%	180 min.	69%	3 days	Most severe pathology in brain and heart.
19	0.15%	22 min. 54 sec.	not determined	None	No pathology.
20	0.15%	128 min. 49 sec.	52.6%	8 days	Minor pathology in brain.
21	0.15%	177 min. 15 sec.	31.7%	ca. 19 min.	Venous congestion in all organs.
22	0.15%	218 min.	66%	14 days	Marked pathology in brain.
23	0.15%	74 min.	62%	14 days	Minor pathology in brain.
24	0.15%	70 min. 54 sec.	50.1%	24 days	No pathology.
25	15% O_2	40½ min.	----	7 days	No pathology.
26	3% O_2	181 min.	----	3 days	No pathology.
27	No data. Because of technical failure, the animal died at the beginning of the experiment.				